WHAT IS CLAIMED IS:

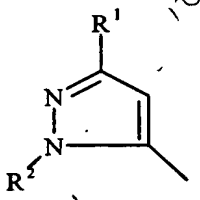
1. A method for the treatment of disease other than cancer mediated by

I

p38 which comprises administering a compound of formula I or a pharmaceutically acceptable salt thereof

wherein A is a heteroaryl selected from the group consisting of

wherein R^1 is selected from the group consisting of C_3-C_{10} alkyl, C_3-C_{10} cycloalkyl, up to per-halosubstituted C_1-C_{10} alkyl and up to per-halosubstituted C_3-C_{10} cycloalkyl;



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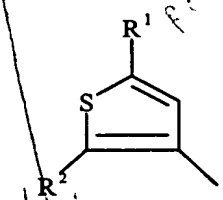

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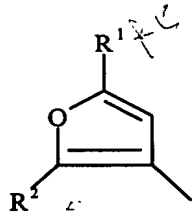


B is a substituted or unsubstituted, up to tricyclic, aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 5- or 6-member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur, wherein if B is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and X_n,

wherein n is 0-3 and each X is independently selected from the group consisting of –CN, CO_2R^5, $-C(O)NR^5R^{5'}$, $-C(O)R^5$, $-NO_2$, $-OR^5$, $-SR^5$, $-NR^5R^{5'}$,

SUB A1

$-NR^5C(O)OR^{5'}$, $-NR^5C(O)R^{5'}$, C_1-C_{10} alkyl, C_{2-10}-alkenyl, C_{1-10}-alkoxy, C_3-C_{10} cycloalkyl, C_6-C_{14} aryl, C_7-C_{24} alkaryl, C_3-C_{13} heteroaryl, C_4-C_{23} alkheteroaryl, substituted C_1-C_{10} alkyl, substituted C_{2-10}-alkenyl, substituted C_{1-10}-alkoxy, substituted C_3-C_{10} cycloalkyl, substituted C_4-C_{23} alkheteroaryl and -Y-Ar;

where X is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of –CN, $-CO_2R^5$, $-C(O)R^5$, $-C(O)NR^5R^{5'}$, $-OR^5$, $-SR^5$, $-NR^5R^{5'}$, $-NO_2$, $-NR^5C(O)R^{5'}$, $-NR^5C(O)OR^{5'}$ and halogen up to per-halosubstitution;

wherein R^5 and $R^{5'}$ are independently selected from H, C_1-C_{10} alkyl, C_{2-10}-alkenyl, C_3-C_{10} cycloalkyl, C_6-C_{14} aryl, C_3-C_{13} heteroaryl, C_7-C_{24} alkaryl, C_4-C_{23} alkheteroaryl, up to per-halosubstituted C_1-C_{10} alkyl, up to per-halosubstituted C_{2-10}-alkenyl, up to per-halosubstituted C_3-C_{10} cycloalkyl, up to per-halosubstituted C_6-C_{14} aryl and up to per-halosubstituted C_3-C_{13} heteroaryl,

wherein Y is - O-, -S-, $-N(R^5)-$, $-(CH_2)_m-$, -C(O)-, -CH(OH)-, $-(CH_2)_mO-$, $-NR^5C(O)NR^5R^{5'}-$, $-NR^5C(O)-$, $-C(O)NR^5-$, $-(CH_2)_mS-$, $-(CH_2)_mN(R^5)-$, $-O(CH_2)_m-$, $-CHX^a-$, $-CX^a{}_2-$, $-S-(CH_2)_m-$ and $-N(R^5)(CH_2)_m-$,

m = 1-3, and X^a is halogen; and

Ar is a 5-10 member aromatic structure containing 0-2 members of the group consisting of nitrogen, oxygen and sulfur which is unsubstituted or substituted by halogen up to per-halosubstitution and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of –CN, $-CO_2R^5$, $-C(O)NR^5R^{5'}$, $-C(O)NR^5$, $-NO_2$, $-OR^5$, $-SR^5$, $-NR^5R^{5'}$, $-NR^5C(O)OR^{5'}$, $-OC(O)R^5$, $-NR^5C(O)R^{5'}$, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_6-C_{14} aryl, C_3-C_{13} heteroaryl, C_7-C_{24} alkaryl, C_4-C_{23} alkheteroaryl, substituted C_1-C_{10} alkyl, substituted C_3-C_{10} cycloalkyl, substituted C_7-C_{24} alkaryl and substituted C_4-C_{23} alkheteroaryl;

wherein if Z is a substituted group, it is substituted by the one or more substituents independently selected from the group consisting of –CN, $-CO_2R^5$, $-C(O)NR^5R^{5'}$, $-OR^5$, $-SR^5$, $-NO_2$, $-NR^5R^{5'}$, $-NR^5C(O)R^{5'}$ and $-NR^5C(O)OR^{5'}$, and

wherein R^2 is C_6-C_{14} aryl, C_3-C_{14} heteroaryl, substituted C_6-C_{14} aryl or substituted C_3-C_{14} heteroaryl,

SUB a1

wherein if R^2 is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and V_n,

wherein n = 0-3 and each V is independently selected from the group consisting of -CN, $-CO_2R^5$, $-C(O)NR^5R^{5'}$, $-OR^5$, $-SR^5$, $-NR^5R^{5'}$, $-C(O)R^5$, $-OC(O)NR^5R^{5'}$, $-NR^5C(O)OR^{5'}$, $-SO_2R^5$, $-SOR^5$, $-NR^5C(O)R^{5'}$, $-NO_2$, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_6-C_{14} aryl, C_3-C_{13} heteroaryl, C_7-C_{24} alkaryl, C_4-C_{24} alkheteroaryl, substituted C_1-C_{10} alkyl, substituted C_3-C_{10} cycloalkyl, substituted C_6-C_{14} aryl, substituted C_3-C_{13} heteroaryl, substituted C_7-C_{24} alkaryl and substituted C_4-C_{24} alkheteroaryl,

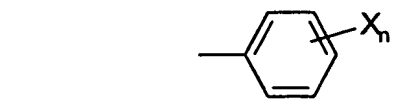
where V is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, -CN, $-CO_2R^5$, $-C(O)R^5$, $-C(O)NR^5R^{5'}$, $-NR^5R^{5'}$, $-OR^5$, $-SR^5$, $-NR^5C(O)R^{5'}$, $-NR^5C(O)OR^{5'}$ and $-NO_2$,

wherein R^5 and $R^{5'}$ are each independently as defined above.

2. A method as in claim 1, wherein R^2 is selected from substituted or unsubstituted members of the group consisting of phenyl and pyridinyl, and the substituents for R^2 are selected from the group consisting of halogen, up to per-halosubstituition and Y_n, wherein n = 0-3, and each Y is independently selected from the group consisting of substituted and unsubstituted C_1-C_6 alkyl, C_3-C_{10} cycloalkyl, C_6-C_{10} aryl, $-NO_2$, $-NH_2$, $-C(O)$-C_{1-6} alkyl, $-C(O)N$-$(C_{1-6}$ alkyl$)_2$, $-C(O)NH$-C_{1-6} alkyl, $-O$-C_{1-6} alkyl, $-NHC(O)H$, $-NHC(O)OH$, $-N(C_{1-6}$ alkyl$)C(O)$-C_{1-6} alkyl, $-N$-$(C_{1-6}$ alkyl$)C(O)$-C_{1-6} alkyl, $-NHC(O)$-C_{1-6} alkyl, $-OC(O)NH$ C_{6-14} aryl, $-NHC(O)O$-C_{1-6} alkyl, $-S(O)$-C_{1-6} alkyl and $-SO_2$-C_{1-6} alkyl,

wherein if Y is a substituted group, it is substituted by one or more halogen, up to per-halosubstitution.

3. A method as in claim 1, wherein B is up to a tricyclic aromatic ring structure selected from the group consisting of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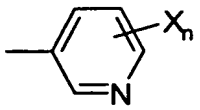
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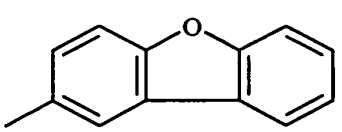
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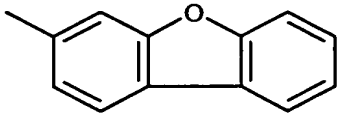
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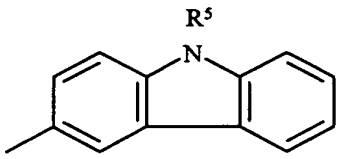
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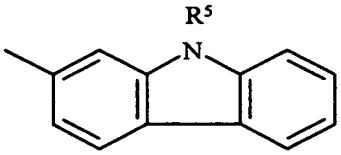

;

which is substituted or unsubstituted by halogen, up to per-halosubstitution, and wherein

n = 0-3 and

each X is independently selected from the group consisting of –CN, $-CO_2R^5$, $-C(O)NR^5R^{5'}$, $-C(O)R^5$, $-NO_2$, $-OR^5$, $-SR^5$, $-NR^5R^{5'}$, $-NR^5C(O)OR^{5'}$, $-NR^5C(O)R^{5'}$, C_1-C_{10} alkyl, C_{2-10}-alkenyl, C_{1-10}-alkoxy, C_3-C_{10} cycloalkyl, C_6-C_{14} aryl, C_7-C_{24} alkaryl, C_3-C_{13} heteroaryl, C_4-C_{23} alkheteroaryl, and substituted C_1-C_{10} alkyl, substituted C_{2-10}-alkenyl, substituted C_{1-10}-alkoxy, substituted C_3-C_{10} cycloalkyl, substituted C_4-C_{23} alkheteroaryl and -Y-Ar;

wherein if X is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of –CN, $-CO_2R^5$, $-C(O)R^5$, $-C(O)NR^5R^{5'}$, $-OR^5$, $-SR^5$, $-NR^5R^{5'}$, $-NO_2$, $-NR^5C(O)R^{5'}$, $-NR^5C(O)OR^{5'}$ and halogen up to per-halosubstitution;

wherein R^5 and $R^{5'}$ are independently selected from H, C_1-C_{10} alkyl, C_{2-10}-alkenyl, C_3-C_{10} cycloalkyl, C_6-C_{14} aryl, C_3-C_{13} heteroaryl, C_7-C_{24} alkaryl, C_4-C_{23} alkheteroaryl, up to per-halosubstituted C_1-C_{10} alkyl, up to per-halosubstituted C_{2-10}-

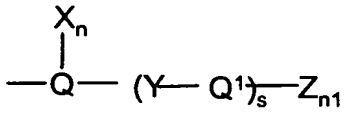
alkenyl , up to per-halosubstituted C_3-C_{10} cycloalkyl, up to per-halosubstituted C_6-C_{14} aryl and up to per-halosubstituted C_3-C_{13} heteroaryl,

wherein Y is - O-, -S-, -N(R^5)-, -(CH_2)-$_m$, -C(O)-, -CH(OH)-, -(CH_2)$_m$O-, -NR^5C(O)NR^5R$^{5'}$-, -NR^5C(O)-, -C(O)NR^5-, -(CH_2)$_m$S-, -(CH_2)$_m$N(R^5)-, -O(CH_2)$_m$-, -CHX^a-, -CX^a_2-, -S-(CH_2)$_m$- and -N(R^5)(CH_2)$_m$-,

m = 1-3, and X^a is halogen; and

Ar is a 5- or 6-member aromatic structure containing 0-2 members of the group consisting of nitrogen, oxygen and sulfur which is unsubstituted or substituted by halogen up to per-halosubstitution and optionally substituted by Z_{n1}, wherein nl is 0 to 3 and each Z is independently selected from the group consisting of –CN, -C(O)R^5, -CO_2R^5, -C(O)NR^5R$^{5'}$, -C(O)R^5, -NO_2, -OR^5, - SR^5, - NR^5R$^{5'}$, -NR^5C(O)O$R^{5'}$, -NR^5C(O)$R^{5'}$, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_6-C_{14} aryl, C_3-C_{13} heteroaryl, C_7-C_{24} alkaryl, C_4-C_{23} alkheteroaryl, substituted C_1-C_{10} alkyl, substituted C_3-C_{10} cycloalkyl, substituted C_7-C_{24} alkaryl and substituted C_4-C_{23} alkheteroaryl; wherein if Z is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of –CN, -CO_2R^5, -C(O)NR^5R$^{5'}$, -OR^5, -SR^5, -NO_2, -NR^5R$^{5'}$, -NR^5C(O)$R^{5'}$ and -NR^5C(O)O$R^{5'}$.

4. A method of claim 1, wherein B is



wherein

Y is selected from the group consisting of –O-, -S-, -CH_2-, -SCH_2-, -CH_2S-, -CH(OH)-, -C(O)-, -CX^a_2, -CX^aH-, -CH_2O- and -OCH_2-,

X^a is halogen,

Q is a six member aromatic structure containing 0–2 nitrogen, substituted or unsubstituted by halogen, up to per-halosubstitution;

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Q^1 is a mono- or bicyclic aromatic structure of 3 to 10 carbon atoms and 0-4 members of the group consisting of N, O and S, unsubstituted or unsubstituted by halogen up to per-halosubstitution,

s = 0 or 1, and

X, Z, n and n1 are as defined in claim 1.

5. A method as in claim 4, wherein

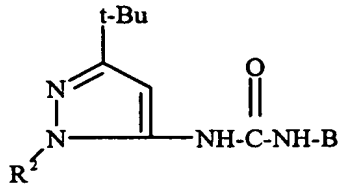
Q is phenyl or pyridinyl, substituted or unsubstituted by halogen, up to per-halosubstitution,

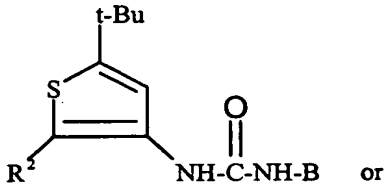
Q^1 is selected from the group consisting of phenyl, pyridinyl, naphthyl, pyrimidinyl, quinoline, isoquinoline, imidazole and benzothiazolyl, substituted or unsubstituted by halogen, up to per-halo substitution, or Y-Q^1 is phthalimidinyl substituted or unsubstituted by halogen up to per-halo substitution, and

Z and X are independently selected from the group consisting of $-R^6$, $-OR^6$ and $-NHR^7$, wherein R^6 is hydrogen, C_1-C_{10}-alkyl or C_3-C_{10}-cycloalkyl and R^7 is selected from the group consisting of hydrogen, C_3-C_{10}-alkyl, C_3-C_6-cycloalkyl and C_6-C_{10}-aryl, wherein R^6 and R^7 can be substituted by halogen or up to per-halosubstitution.

6. A method as in claim 4, wherein Q is phenyl, Q^1 is phenyl or pyridinyl, Y is –O-, -S- or $-CH_2$-, and X and Z are independently Cl, F, CF_3, NO_2 or CN.

7. A method as in claim 1, which comprises administering a compound of one of the formulae or a pharmaceutically acceptable salt thereof:





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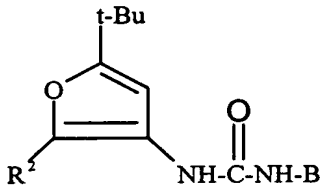

wherein B and R^2 are as defined in claim 1.

8. A method as in claim 7, wherein R^2 is selected from substituted and unsubstituted members of the group consisting of phenyl and pyridinyl, wherein if R^2 is a substituted group, it is substituted by one or more substituents selected from the group consisting of halogen and W_n, wherein n = 0-3, and W is selected from the group consisting of $-NO_2$, $-C_{1-3}$ alkyl, $-NH(O)CH_3$, $-CF_3$, $-OCH_3$, -F, -Cl, $-NH_2$, -OC(O)NH up to per-halosubstituted phenyl,_$-SO_2CH_3$, pyridinyl, phenyl, up to per-halosubstituted phenyl and C_1-C_6 alkyl substituted phenyl.

9. A method as in claim 1, comprising administering an amount of compound of formula I effective to inhibit p38.

10. A method as in claim 1, wherein the compound of formula I displays p38 activity (IC_{50}) better than 10μM as determined by an in-vitro kinase assay.

11. A method according to claim 1, wherein the disease is mediated by a cytokine or protease regulated by p38.

12. A method according to claim 1, wherein R^2 is t-butyl.

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13. A method according to claim 1, comprising administering an amount of a compound of formula I effective to inhibit p38.

14. A method according to claim 1, comprising administering an amount of a compound of formula I effective to inhibit production of a disease-mediating cytokine or protease.

15. A method according to claim 1, wherein the disease is an inflammatory or immunomodulatory disease.

16. A method according to claim 1, wherein the disease is rheumatoid arthritis, osteoarthritis, osteoporosis, asthma, septic shock, inflammatory bowel disease, or the result of host-versus-graft reactions.

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